REMARKS

Applicants appreciate the thorough examination of the present application as evidenced by the Office Action dated November 17, 2004 ("Office Action"). Claims 1, 3-21, 23-40, 42, 43 and 45-54 are pending in the present application upon entry of the present Amendment. Claims 1, 50, 52 and 54 have been amended herein. New Claim 55 has been added. Support for the claim amendments and new claim can be found in the specification and claims as originally filed. The specification has been amended to include updated priority information. Applicants respectfully submit that these amendments and new claim do not present new matter, and respectfully request entry thereof. The concerns raised by the Examiner are addressed below as set forth in the Office Action.

I. Consideration of References Cited on Form PTO-1449

Applicants will attempt to locate complete citations for Downey et al. (no. 26) and Toh et al. (no. 60) cited on Form PTO-1449 filed December 19, 2001. Upon location of the complete citations, Applicants will submit an Information Disclosure Statement to provide this information.

II. Claim Rejections Under 35 U.S.C. § 112, First Paragraph, Enablement Rejection

Claims 1, 3-21, 23-40, 42-43 and 45-54 stand rejected under 35 U.S.C. § 112, first paragraph, as lacking enablement. *See* Office Action, page 2. Applicants respectfully disagree with this assertion.

On page 2, the Office Action indicates that the specification enables the following:

> [A] method for diagnosis of disseminated intravascular coagulation (DIC) comprising the steps of (a) adding a metal divalent ion and one or more clot inhibitor to a blood sample from a patient to cause the formation of a complex comprising C reactive protein and at least one human lipoproteins selected from the group consisting of VLDL and IDL, while causing no fibrin polymerization, (b) measuring the formation of said complex over time so as to derive a time-dependent measurement profile, and d) correlating the formation of the

> precipitate to the likelihood of mortality, the greater the formation of said complex, the greater the likelihood of death of the patient.

In an effort to expedite allowance of some of the pending claims, Applicants have amended Claim 50 to include the majority of the recitations noted above. Applicants respectfully submit that one reasonably skilled in the art, i.e., cardiovascular physiology, would be able to diagnosis "hemostatic dysfunction," defined herein as "a condition evidenced by the formation of a precipitate (prior to or in the absence of clot formation, depending upon the reagent used)" (Present Application, page 11, lines 29-32) on the basis of the present disclosure without undue experimentation, particularly in view of the information known in the art regarding the well-known term "hemostatic dysfunction." Thus, Claim 50 is directed to a method of diagnosing "hemostatic dysfunction." Claim 51 is directed to a method of Claim 50, wherein the hemostatic dysfunction is disseminated intravascular coagulation (DIC). New Claim 55 recites that the metal divalent ion of Claim 50 is calcium.

Applicants reiterate that it is only required that the specification teach ***one skilled in the art*** how to make and use the claimed invention. The issue is not whether some experimentation is necessary to optimize the invention; the relevant question is whether the amount of experimentation is "undue." In view of the claim amendments and remarks set forth above, Applicants respectfully submit that one skilled in the art relevant to the present invention would be able to (a) diagnose hemostatic dysfunction as recited in Claim 50, and claims dependent therefrom, and (b) test the effectiveness of a therapeutic for treatment of hemostatic dysfunction as recited in Claim 52, without "undue" experimentation.

Accordingly, Applicants respectfully submit that Claims 1, 3-21, 23-40, 42-43 and 45-54 are patentable. Applicants further submit that Claims 50-55 are separately patentable in view of the claim amendments and respectfully request that the enablement rejection of these claims be withdrawn.

III. Claim Rejections Under 35 U.S.C. § 112, First Paragraph, Written Description Rejection

Claims 1, 3-21, 23-40, 42-43 and 45-54 stand rejected under 35 U.S.C. § 112, first paragraph, as lacking written description. *See* Office Action, page 5. In particular, the Office Action states that "[t]he specification does not reasonably provide a written description of *any* one or more "reagents" (claims 1, 18, 20, 32, 40 and 49), *any* inhibiting reagent (claim 32), *any* antibody capable of binding to *any* lipoprotein-acute phase protein binding site (claim 36) for a method of diagnosing *any* "condition" of the patient (Claim 1) or a method for testing the effectiveness of any therapeutic (claim 49)." Office Action, page 5, emphasis omitted. Applicants respectfully disagree with these assertions.

Applicants respectfully submit that "[w]hat is conventional or well known to one of ordinary skill in the art need not be disclosed in detail. If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met." Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, first paragraph, "Written Description" Requirement, 66 Fed. Reg. 1099, 1106 (Jan. 5, 2001). On this basis, Applicants respectfully assert that the recitations of Claims 1, 3-21, 23-40, 42-43 and 45-54 alleged to lack written description would be understood by one of ordinary skill in the art and appreciated as having been in possession of the inventors at the time of filing by the skilled artisan.

However, in order to facilitate allowance of some of the pending claims, Claim 50 has been amended, as noted above, as well as Claim 52 to incorporate recitations noted in the Office Action. *See* Office Action, page 2 and page 7.

Accordingly, Applicants respectfully submit that the pending claims, in particular, Claims 50-55, comply with the written description requirement under 35 U.S.C. § 112, first paragraph, and respectfully request withdrawal of these rejections.

IV. Claim Rejection Under 35 U.S.C. § 112, Second Paragraph, Indefiniteness Rejection

Claims 1, 3-17, 49 and 52 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention, and more particularly for omitting essential steps. *See* Office Action, page 6.

Applicants have amended Claims 1, 49 and 52 to include the recitations suggested in the Office Action on pages 6-7. Accordingly, Applicants respectfully submit that Claims 1, 49 and 52, and claims dependent therefrom, are not indefinite under 35 U.S.C. § 112, second paragraph, as being incomplete for omitting essential steps and respectfully request that the rejection of these claims be withdrawn.

V. Claim Rejections Under 35 U.S.C. § 102

Claims 1, 3-21, 23-39 and 49-54 stand rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 6,429,017 to Toh et al. Applicants respectfully disagree with this assertion.

Applicants note that U.S. Patent Application Serial No. 09/372,954, now issued U.S. Patent No. 6,429, 017 (hereinafter, the "'017 patent"), appears in the priority statement for the present application. Applicants respectfully submit that the '017 patent fails to teach each and every recitation of Claims 1, 3-21, 23-39 and 49-54 as required to establish anticipation under 35 U.S.C. § 102. In fact, the Office Action states that "the conflicting claims [Claims 1, 3-21, 23-39 and 49-54 and Claims 1-35 of the '017 patent] are not identical . . . The claims of the '017 patent are drawn to a generic method of diagnosing hemostatic dysfunction by adding a reagent such as calcium to a test sample and determining the complex formation of C-reactive protein." Office Action, page 10. Consequently, each and every recitation of Claims 1, 3-21, 23-39 and 49-54 is not disclosed by the '017 patent. In particular, the claims of the '017 patent do not teach each and every recitation of independent Claims 1, 18, 32, 49, 50, 52 and 54.

Accordingly, Applicants respectfully submit that Claims 1, 3-21, 23-39 and 49-54 are not anticipated under 35 U.S.C. § 102(e) in view of the '017 patent, and respectfully request that these rejections be withdrawn.

VI. Claim Rejection Under 35 U.S.C. § 103

Claims 40 and 42-48 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over the '017 patent as evident by Cabana et al. *J Immunol* **130(4)**: 1736-1742 (1983) in view of Richter et al. *Clinica Chemica Acta* **261**: 141-148 (1997). Applicants respectfully disagree with this assertion.

Case law holds that the mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. M.P.E.P. §2143.01, citing *In re Mills*, 916 F.2d 680, 16 U.S.P.Q.2d 1430 (Fed. Cir. 1990). The Court of Appeals for the Federal Circuit has stated that, to support combining or modifying references, there must be **particular** evidence from the prior art as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed. *In re Kotzab*, 55 U.S.P.Q.2d 1313, 1317 (Fed. Cir. 2000). Applicants respectfully submit, that in this instance, one of ordinary skill in the art **would not** have been motivated to combine these particular references.

The Office Action states "[o]ne having ordinary skill in the art would have been motivated to do this [add any acute phase protein such as CRP] because Cabana et al. teach CRP forms complex with VLDL. Richter et al. teach the amount of complex depends on the amount of CRP in the present calcium. Further, it is an obvious variation of the teaching of the '017 patent by adding an acute phase protein as one of the reagents to determine the amount of VLDL or complex formation in the test sample knowing that CRP forms a complex with VLDL." Office Action, page 9.

For reasons discussed above, the '017 patent does not teach the recitations of Claim 40, and the cited references do not cure the deficiencies. Moreover, in contrast to the assertions of the Office Action, it is ***not*** an obvious variation of the '017 patent

to add an acute phase protein as recited in the instant claims where none of the cited references suggest such addition, and more importantly, such addition in combination with the steps recited in Claim 40.

Applicants respectfully submit that it is ***only*** through impermissible hindsight combined with picking and choosing portions of the cited references to the exclusion of deficient and/or divergent teachings is one of ordinary skill in the art able to arrive at the present invention recited in Claim 40.

Accordingly, Applicants respectfully submit that Claims 40 and 42-48 are not obvious under 35 U.S.C. § 103(a) in view of the cited references, and respectfully request that these rejections be withdrawn.

VII. Claim Rejections Under the Judicially Created Doctrine of Obviousness-Type Double Patenting

Claims 1, 3-21, 23-39 and 49-54 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1-35 of the '017 patent. *See* Office Action, page 10.

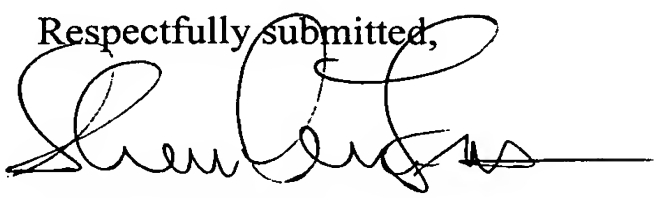
Upon indication by the Examiner during the telephone interview requested herein that some, if not all, of Claims 1, 3-21, 23-39 and 49-54 are allowable, but for the rejection of these claims under the obviousness-type double patenting rejection, Applicants will promptly submit a terminal disclaimer in order to expedite allowance of the potentially allowable claims.

Conclusion

Applicants respectfully submit that, for the reasons discussed above, the claims are enabled and supported by the written description in the specification, and that the cited references in the present rejections do not disclose or suggest the present invention as claimed. As noted above, however, Applicants respectfully request that a

telephone interview between the Examiner and the undersigned be granted prior to the issuance of an official action. The Examiner may contact the undersigned at (919) 854-1400.

Respectfully submitted,



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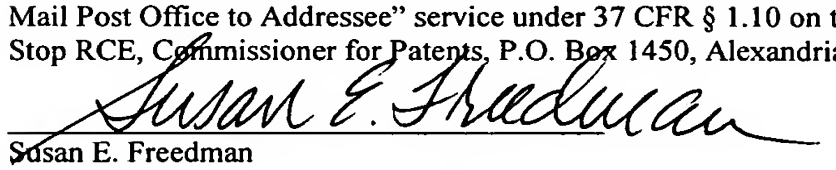

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